

We claim:

Sub 31
~~1. A spectroscopic method of analyzing a sample, comprising:~~

5 irradiating a sample with radiation to produce return radiation from the sample, wherein the return radiation is modulated by the sample;

 monitoring a first portion of the modulated return radiation at a first distance from the sample;

10 monitoring a second portion of the modulated return radiation at a second distance from the sample;

 processing the first and second portions of the modulated return radiation to determine a modulation characteristic of the sample.

2. The method of claim 1, wherein the radiation comprises substantially monochromatic light.

3. The method of claim 1, wherein the radiation comprises laser light.

[4. The method of claim 1, wherein the radiation is selected to induce fluorescence in the sample.

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 5. The method of claim 1, wherein irradiating the sample comprises directing radiation at the sample using a waveguide.

⁵ 5. The method of claim ⁴ 5, wherein the waveguide is an optical fiber.

⁶ 6. The method of claim ⁴ 5, wherein the waveguide is an optical fiber bundle.

Sub A57 [8. The method of claim ~~1~~ 1, wherein the return radiation is modulated by attenuation.

³¹ 9. The method of claims ³⁰ 8, wherein the return radiation is attenuated by scattering.

³² 10. The method of claim ³⁰ 8, wherein the return radiation is attenuated by absorption.

11. The method of claim ~~1~~ 1, wherein the return radiation comprises fluorescence of the sample.

Sub B2 12. The method of claim 1, wherein monitoring of the modulated return radiation comprises:

collecting a portion of the modulated return radiation;
and

determining the intensity of the collected portion of modulated return radiation.

13. The method of claim 12, wherein the first portion of the modulated return radiation is collected with a first waveguide and the second portion of the modulated return radiation is collected with a second waveguide.

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14. The method of claim 13, wherein the first waveguide is an optical fiber.

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15. The method of claim 13, wherein the first waveguide is an optical fiber bundle.

11 8
16. The method of claim 13, wherein the second waveguide is an optical fiber.

12 8
17. The method of claim 13, wherein the second waveguide is an optical fiber bundle.

Sub B3
18. The method of claim 1, wherein irradiating the sample comprises directing radiation to the sample using a first waveguide and wherein the return radiation is monitored using the first waveguide.

19. The method of claim 12, wherein the intensity of the collected portion of the return radiation is determined with a sensor.

20. The method of claim 12, wherein the intensity of the first portion of the modulated return radiation is determined with a sensor.

21. The method of claim 12, wherein the intensity of the second portion of the modulated return radiation is determined with a sensor.

22. The method of claim 12, wherein the intensity of the first portion of the modulated return radiation is determined with a first sensor and the intensity of the second portion of the modulated return radiation is determined with a second sensor.

23. The method of claim 12, wherein the first and second portions of the modulated return radiation are measured consecutively.

24. The method of claim 12, wherein the first and second portions of the modulated return radiation are measured simultaneously.

25. The method of claim 8, wherein the modulation characteristic of the sample is attenuation.

26. The method of claim 8, wherein the modulation characteristic of the sample is absorption.

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27. The method of claim ³⁰~~8~~, wherein the modulation characteristic of the sample is optical rotation.

³⁵
28. The method of claim ³⁴~~26~~, wherein the method further includes determining transmittance.

²⁰
29. The method of claim ¹¹~~1~~, wherein the method further includes determining the intrinsic fluorescence of the sample.

²¹
30. The method of claim 1, wherein the sample is biological material.

²²
31. The method of claim ²¹~~30~~, wherein the biological material is living tissue.

Sub A6 > [32. The method of claim 29, wherein the method further includes determining a physiological property of the biological material using the modulation characteristic.

33. The method of claim 30, wherein the method further includes determining a physiological property of the tissue using the modulation characteristic.

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34. The method of claim ²⁵~~33~~, wherein the physiological property of the tissue is tissue oxygenation.

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35. The method of claim 33, wherein the physiological property of the tissue is hypoxia.

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36. The method of claim 36, wherein the method further includes determining a pathological property of the biological material using the modulation characteristic.

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37. The method of claim 37, wherein the method further includes determining a pathological property of the tissue using the modulation characteristic.

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38. The method of claim 38, wherein the pathological property of the tissue is the malignant condition of the tissue.

Sub B

39. A spectroscopic method for determining the oxygenation of a biological material, comprising:

irradiating a sample of a biological material with radiation to produce return radiation from the sample, wherein the return radiation is modulated by attenuation of the sample;

monitoring a first portion of the modulated return radiation at a first distance from the sample;

monitoring a second portion of the modulated return radiation at a second distance from the sample;

processing the first and second portions of the modulated return radiation to determine the attenuation of the sample;

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determining oxygenation of the sample using the attenuation of the sample.

Sub A8

40. The method of claim 39, wherein the oxygenation of the sample is determined by comparing the attenuation of the sample to the attenuation of a sample having a known level of oxygenation.

Sub B5

41. A spectroscopic method for determining the concentration of hemoglobin in a biological material, comprising:

irradiating a sample of a biological material with radiation to produce return radiation from the sample, wherein the return radiation is modulated by attenuation of the sample;

monitoring a first portion of the modulate return radiation at a first distance from the sample;

monitoring a second portion of the modulated return radiation at a second distance from the sample;

determining the concentration of hemoglobin in the sample using the attenuation of the sample.

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42. The method of claim 41, wherein the concentration of hemoglobin is determined by comparing the attenuation of the sample to the attenuation of a sample having a known concentration of hemoglobin.

Sub A9

43. A method for determining the oxygenation of a sample, comprising:

determining the transmittance of the sample at plurality of wavelengths;

5 determining the wavelength of peak transmittance in the 450-500 nm range;

comparing the wavelength of peak transmittance to the wavelength of peak transmittance of a sample having a known level of oxygenation.

44. A spectroscopic method for the detection of ischemia in a biological sample, comprising:

determining the shape of the fluorescence spectrum of a biological sample;

5 identifying a main lobe of the fluorescence spectrum in the wavelength range 350-450 nm;

determining the symmetry of the main lobe.

45. The method of claim 44, wherein the symmetry of the main lobe is determined using skewness.

46. The method of claim 45, wherein a small skewness value indicates that the lobe is symmetric.

47. A method for determining a physiological property of a biological sample, comprising:

determining the intrinsic fluorescence of the sample;

determining a physiological property of the sample using the intrinsic fluorescence.

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Sub B6 48. A method for determining a physiological characteristic of a biological material, comprising:

irradiating a sample of a biological material with radiation to produce return radiation from the sample, wherein the return radiation is modulated by the sample;

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monitoring a first portion of the modulated return radiation at a first distance from the sample;

monitoring a second portion of the modulated return radiation at a second distance from the sample;

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processing the first and second portions of the modulated return radiation, using a predictive model, to determine a physiological characteristic of the sample.

Sub A10 49. The method of claim 48, wherein the predictive model is a multivariate linear regression.

Sub B7 50. A method for determining a physiological characteristic of a biological material, comprising:

irradiating a sample of a biological material with radiation to produce return radiation from the sample, wherein the return radiation is modulated by the sample;

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monitoring a first portion of the modulated return radiation at a first distance from the sample;

monitoring a second portion of the modulated return radiation at a second distance from the sample;

10 processing the first and second portions of the modulated return radiation to determine a modulation characteristic of the sample

processing the modulation characteristic using a predictive model to determine a physiological characteristic of the sample.

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51. The method of claim 48, wherein the predictive model is a multicriteria associative memory classifier.

52. Apparatus for analyzing a sample, comprising:

a source adapted to emit radiation that is directed at a sample to produce return radiation from the sample, wherein the return radiation is modulated by the sample;

5 a first sensor, displaced by a first distance from the sample, adapted to monitor the return radiation and generate a first signal indicative of the intensity of the return radiation;

10 a second sensor, displaced by a second distance from the sample volume, adapted to monitor the return radiation and generate a second signal indicative of the intensity of return radiation; and

15 a processor associated with the first sensor and the
second sensor and adapted to process the first and second
signals to determine a modulation characteristic of the
sample.

53. Apparatus for analyzing a sample, comprising:

5 a source adapted to emit radiation that is directed at a
sample volume in a sample to produce return light from the
sample, such return light including modulated return light
resulting from modulation by the sample;

10 a first sensor, displaced by a first distance from the
sample volume adapted to monitor the return light and generate
a first signal indicative of the intensity of return light;
and

15 a second sensor, displaced by a second distance from the
sample volume adapted to monitor the return light and generate
a second signal indicative of the intensity of return light;

20 a processor associated with the first sensor and the
second sensor and adapted to process the first and second
signals to determine a modulation characteristic of the
sample.

54. Apparatus for determining a modulation
characteristic of a biological material, comprising:

a source adapted to emit excitation light;

5 a first waveguide disposed a first distance from the
sample adapted to transmit the excitation light from the light

source to the biological material to cause the biological material to produce return light and adapted to collect a first portion of the return light, such return light including fluorescence of the biological material;

10 a first sensor, associated with the first waveguide, adapted to measure the intensity of the first portion of the return light;

15 a second waveguide disposed at a second distance from the sample adapted to collect a second portion of the return light;

20 a second sensor, associated with the first waveguide, adapted to measure the intensity of the second portion of the return light; a processor adapted to process the first and second signals to determine a modulation characteristic of the biological material.

Sub B8 55. Apparatus for analyzing a sample, comprising:

a source adapted to emit radiation that is directed at a sample volume in a sample to produce return light from the sample, such return light including modulated return light resulting from modulation by the sample;

a first sensor, displaced by a first distance from the sample volume adapted to monitor the return light and generate a first signal indicative of the intensity of the return light; and

a second sensor, displaced by a second distance from the sample volume adapted to monitor the return light and generate

a second signal indicative of the intensity of return light;
a processor associated with the first sensor and the second sensor and adapted to process the first and second signals to determine a physiological property of the sample.

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56. Apparatus for determining a physiological property of biological material, comprising:

a source adapted to emit excitation light;

5 a first waveguide disposed a first distance from the sample adapted to transmit the excitation light from the light source to the biological material to cause the biological material to produce return light and adapted to collect a first portion of the return light, such return light including fluorescence of the biological material;

10 a first sensor, associated with the first waveguide, for measuring the intensity of the first portion of the return light;

15 a second waveguide disposed at a second distance from the sample adapted to collect a second portion of the return light;

20 a second sensor, associated with the first waveguide, for measuring the intensity of the second portion of the return light; a processor adapted to process the first and second signals to determine a physiological property of the biological material.

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